

### C. Remarks

The numbered paragraphs below correspond to the numbered paragraphs of the Official Action. The Applicants respectfully request reconsideration in light of the present amendments and remarks.

3. The Applicants respectfully disagree with the Examiner's objection that the specification does not reasonably provide enablement for preventing stereotypy.

#### The Quantity of Experimentation Necessary

The Examiner states the example failed to study animals that have not started to show crib-biting behaviour. The Examiner is respectfully advised that seven non-crib-biting foals (control foals) were studied. Four of these foals were allocated a typical base diet, and three were allocated an antacid diet (page 10, lines 26-27, and 34-35).

#### The Amount of Direction or Guidance Presented

The Examiner also states there is no guidance given for preventing crib-biting behaviour. The Applicants respectfully disagree. The present specification, on page 7, lines 28-30, specifies, "In order to minimise the risk of an animal developing a stereotypy, the animal may be treated with a composition or method according to the invention from birth." On page 18, lines 22-24, the present specification reads, "Compositions and methods according to the invention may be particularly effective at preventing stereotypy when the animal being treated is a weaning or recently weaned animal".

The reasons why compositions and methods of the invention are thought to be effective in preventing stereotypy are explained in the present specification on page 19, lines 6-22, wherein it reads,

[T]he realisation that low stomach pH is linked with stereotypic behaviour suggests that pain caused by low stomach pH may cause the animal to perform a stereotypy, such as crib-biting, to stimulate the flow of saliva into the stomach. This saliva would be expected to increase stomach pH and alleviate the pain. The fact that significant numbers of horses develop stereotypic behaviour during the immediate post-weaning period may be because the diet of a foal changes significantly during weaning. If such a dietary change results in a persistent decrease in stomach pH, then stereotypic behaviour may be more likely to occur. Administration of compositions according to the invention to an animal, especially a weaning or recently weaned animal, may ensure that its stomach pH is not persistently low and remove, therefore, the need for the animal to stimulate the flow of saliva into the stomach.

This explanation is supported by the experimental data. The specification on page 17, lines 9-11, states the results presented, “demonstrate for the first time a relationship between stomach condition and abnormal oral behaviour in the horse”. On page 17, lines 15-23, it is stated, “[t]he general appearance of the stomach of the crib-biting foals supports the hypothesis that their stomachs are more acid. The results also show that an improvement in stomach condition was associated with reduced crib-biting behaviour. . . . Foals whose mild ulceration cleared showed

the greatest improvement in crib-biting. In some of these foals crib-biting ceased altogether.”

From these results it is clear to a person of ordinary skill in the art that maintaining good stomach condition by controlling stomach pH can be expected to prevent crib-biting.

#### The Predictability or Unpredictability

As previously discussed, the example includes non crib-biting animals, and the present application describes how crib-biting may be prevented and provides experimental evidence in support of the underlying theory.

#### The Breadth of the Claims

The Applicants believe the specification teaches a skilled artisan how crib-biting may be prevented; therefore, the scope of the claims is commensurate with the disclosure.

4. The Applicants believe it is clear from the specification how stomach pH of the animal is controlled. Page 5 of the specification reads, “stomach pH of the animal may be controlled by administering a composition according to the invention to the animal”. Page 19, lines 22-27 of the specification read, “[i]t is believed that the fibre may help to prolong the time spent chewing by an animal. This in turn prolongs the production of saliva which neutralises stomach acid. The fat is thought to delay emptying of the stomach so that the beneficial effect of the antacid and/or fibre is prolonged”. Page 6, line 32 to page 7, line 9 describe suitable stomach antacids for use in compositions and methods of the invention. The Example (pages 8-18) describes administration of Neigh-Lox.

5-9. The Examiner's suggested amendments to Claims 3-5, and 8, have been incorporated into the present claim amendments.

10. Claim 11 has been amended to specify: "A method of treatment, prevention, or amelioration of animal stereotypy which comprises controlling stomach pH of an animal by administering to the animal a stomach antacid, to treat, prevent or ameliorate stereotypy in the animal."

It is respectfully submitted that amended claim 11 meets all the requirements of 35 U.S.C. § 112.

New Claim 34, which finds support in original Claim 19 (now canceled), has been added by way of the present amendment. New Claim 34 reads, "A method of treatment, prevention, or amelioration of animal stereotypy which comprises controlling stomach pH of an animal by administering to the animal a composition comprising fat, fibre, and optionally, a stomach antacid, to treat, prevent or ameliorate stereotypy in the animal."

11-17. Claim 1 has been amended to read, "[a] composition for use in the treatment, prevention, or amelioration of animal stereotypy which comprises fat, fibre, and a stomach antacid." It is respectfully submitted that the claim as amended is patentable over the documents cited by the Examiner.

The Winskill reference ("Winskill") relates to the effect of a foraging device (a Foodball) on the behaviour of the stabled horse. As the Examiner acknowledges at the end of the second paragraph in point 17 of the Official Action, it does not teach a feed composition that contains an antacid. Accordingly, Claim 1, as amended, is not anticipated by Winskill.

The Examiner calculates that Winskill discloses about 48.5% for the amount of fibre and about 6.7% for the amount of fat in the compositions. The Examiner's calculations

appear to be based on the amounts of fibre and fat present as a percentage of the total amount of protein (100g), fibre (200g), oil (27.5g) and ash (85g). However, Winskill, on page 28, line 1, states that each kilogram of the food contains these amounts. Accordingly, the correct percentages are 20% fibre and 2.75% oil.

The Examiner also states, “[t]he horses in Winskill exhibited stereotypic behaviour”. The Applicants respectfully disagree. In Winskill, on page 34, lines 4-5, it is explicitly stated, “none of the horses used for the experiment were seen to perform stereotypic behaviours”.

Winskill, in relation to stereotypic behaviours, discloses, “the Foodball could have a possible role for their treatment or prevention” (page 34, line 5). However, Winskill only attaches significance to the behavioural aspects associated with use of the Foodball, and not to the Foodball’s content. The abstract states that stereotypies may be caused by the inability of horses to express foraging behaviour. On page 34, lines 16-17, Winskill concludes, “the Foodball appears to be a useful behavioural enrichment device for stabled horses” (*emphasis provided*). Accordingly, Winskill teaches that physical use of a Foodball rather than administration of a fat and fibre diet could have a possible role in the treatment or prevention of stereotypies. Therefore, it is respectfully submitted that, from the teaching of Winskill, a person of ordinary skill in the art would not be led to believe that administering a fat and fibre diet to the animal would treat or prevent stereotypy.

It is further submitted that one of ordinary skill in the art cannot combine Winskill with the Johnson references (“Johnson”), or the Pagan reference (“Pagan”) to provide a composition falling within the scope of amended Claim 1 since the teaching of Winskill relates to use of behavioural enrichment devices for the possible treatment of stereotypies, rather than

dietary enrichment.

As noted by the Examiner, Johnson on page 139, right column, first complete paragraph, last four lines, states, “neutralising the acidity of the hind-gut of such animals by administering sodium carbonate to the caecum lowered the incidence of stereotypic behaviour, suggesting that acidity in the lower gut may be a stimulus to such behaviour”. This passage summarises the results of a study by Willard *et al.* (Johnson, page 139, right column, first complete paragraph, lines 10-14). The sodium carbonate referred to was administered by caecal infusion in order to increase caecal pH (Willard, page 87, left column, first paragraph, lines 3-4, and second paragraph, lines 1-2). As also noted by the Examiner, Johnson hypothesised “that a relationship might exist between behavioural responses and pH of the hindgut” (page 139, right column, second complete paragraph, last two lines).

The Applicants respectfully submit that identification of a link between hind-gut acidity and stereotypy would not have led one of ordinary skill in the art to the conclusion that there is also a link between stomach acidity and performance of abnormal behaviour. As explained below, hindgut pH and stomach pH have a different chemical basis and are not dependent on each other. Different agents are used to increase hindgut pH and stomach pH. The Applicants submit that a person of ordinary skill in the art seeking to increase hindgut pH to treat stereotypy would not have thought to administer a stomach antacid based upon the teachings of the cited art.

The hind-gut consists of the colon and caecum. As shown in the attached figure and table from “Feeding and Nutrition of Horses”, by J. Kohnke (1998), the volume of fluid in the digestive system changes significantly as food passes from the stomach to the hind-gut (7.5-15 litres in the stomach, 40-50 litres in the small intestine, 25-30 litres in the caecum, 50-60 litres

in the large colon, and 18-19 litres in the small colon); and, it takes several days for processed food to reach the rectum. There is also a change in pH along the digestive system from acidic in the stomach, to alkaline in the small intestine, to neutral/acidic in the hind-gut (Argenzio, *et al.* (1974) Am J Physiol 226, page 1048). WO 96/20709 explains (at page 1, lines 23-29, and page 5, lines 7-9) that abnormal acidity in the hind-gut is caused by rapid bacterial fermentation of starch, sugar, or other carbohydrate which leads in particular to the accumulation of lactic acid.

In contrast, the primary cause of stomach acidity is secretion of acid into the stomach. Thus, acidity in the hind-gut has a different chemical basis from stomach acidity. These volume and pH changes, the length of time taken for food to travel through the digestive system, and the different chemical basis for stomach and hind-gut acidity means that stomach and hind-gut pH are not directly dependent on each other.

A person of ordinary skill in the art seeking to increase hind-gut pH would not have provided a composition comprising a stomach antacid. Further, if the skilled artisan desired to increase hind-gut pH with sodium carbonate, the sodium carbonate would not have been administered to the stomach since it would not be expected to have any effect in the hind-gut, either due to dilution or chemical break-down. Rowe, *et al.*, International Horse Industry Symposium, RIRDC, 2001, on the left page, point 4, states, "Buffers such as sodium bicarbonate are unlikely to reach the hindgut as the acidic conditions in the stomach convert all bicarbonate to carbon dioxide and water". In Willard, caecal pH was increased by infusions of sodium carbonate into the caecum, rather than by administering sodium carbonate to the stomach.

Accordingly, it is respectfully submitted that knowledge that caecal infusion of sodium carbonate to increase hind-gut pH might lower the incidence of stereotypic behaviour would not have encouraged one of ordinary skill in the art to include an antacid with fat and fibre

to form a stomach-administered composition for the treatment of stereotypy with a reasonable expectation of success.

Pagan describes treatment and prevention of ulcers in horses. The reference contains no disclosure of a link between stomach condition and performance of abnormal behaviour. The Applicants submit that one of ordinary skill in the art would not have been motivated to combine Pagan with Winskill to provide a composition falling within the scope of Claim 1, as amended.

That it is obvious to link stomach acidity with stereotypic behaviour because it is known there is a link between caecal/hindgut pH and behaviour of horses is improper hindsight. The proposed involvement of caecal/hind-gut pH is only one of many other theories (e.g., lack of environmental stimulation, frustration of natural behavioural drives, imitation of other horses, inherited traits) (*see also*, Johnson, page 139, second column, first paragraph).

Stomach and hind-gut acidity have a different chemical basis and are not dependent upon each other. It is submitted that knowledge of the link between hind-gut acidity and abnormal behaviour in the cited art would not have led one of ordinary skill in the art to administer a stomach antacid, either alone or with fat and fibre, to treat stereotypy. Therefore, the Applicants respectfully request withdrawal of the rejections over the cited.

18. Claim 11 has been amended to specify “A method of treatment, prevention, or amelioration of animal stereotypy which comprises controlling stomach pH of an animal by administering to the animal a stomach antacid, to treat, prevent or ameliorate stereotypy in the animal.”

New Claim 34 (previous claim 19) has been added and reads, “A method of treatment, prevention, or amelioration of animal stereotypy which comprises controlling stomach



pH of an animal by administering to the animal a composition comprising fat, fibre, and optionally, a stomach antacid, to treat, prevent or ameliorate stereotypy in the animal.”

The Applicants respectfully submit the methods of Claims 11 and 34 are patentably distinguishable over the disclosure of the documents cited by the Examiner. Specifically, as explained hereinbefore, stomach acidity and hindgut pH have a different chemical basis and are not dependent on each other. To re-summarize, identification of a link between hind-gut acidity and reduced incidence of stereotypic behaviour would not lead one of ordinary skill in the art to the conclusion that there is also a link between stomach acidity and performance of abnormal behaviour. As a result, one of ordinary skill in the art would not have been led to treat stereotypy by controlling stomach pH. Johnson, therefore cannot render obvious the presently-pending claims, either alone or in combination with Winskill.

As pointed out hereinbefore in relation to objection paragraph 17, the sodium carbonate referred to in the right column of page 139 of Johnson was administered by infusion into the caecum in order to increase caecal pH. If the antacid were administered orally, it would not be expected to have any effect in the hind-gut, either due to dilution or chemical break-down by the time it reached the hindgut. Thus, there is no motivation for the skilled artisan to administer sodium carbonate to the stomach. Indeed, from the teachings of the cited art, it would be expected that this would have no effect on hindgut pH and, therefore, no effect on incidence of stereotypy.

As noted above, Winskill discloses the effect of a Foodball containing food with 20% fibre and 2.75% oil on the behaviour of the stabled horse. However, since the reference explicitly states on page 34, lines 4-5, that “ none of the horses used for the experiment were seen to perform stereotypic behaviours”, the document cannot anticipate the method claims of the

present application. Further, Winskill, on page 34, lines 16-17, concludes, “the Foodball appears to be a useful behavioural enrichment device for stabled horses” and only, therefore, attaches significance to the behavioural aspects associated with use of the Foodball, and not to its content. Winskill, therefore cannot render obvious the presently-pending claims, either alone or in combination with Johnson.

The Applicants submit a person of ordinary skill in the art would not, by the teachings of Winskill, be motivated to administer a fat and fibre diet to an animal for the treatment or prevention of stereotypy. It is therefore submitted that new Claim 34 is not rendered obvious by the disclosure of this document.

Pagan does not disclose a link between stomach condition and performance of abnormal behaviour. While the Examiner states, “it would have been obvious to one of ordinary skill in the art at the time the invention was made to use histamine type-2 antagonists or proton pump inhibitor . . . in place of the sodium carbonate suggested by Johnson”, a skilled artisan would not be motivated to administer agents that have an effect in the stomach in place of a caecal infusion of sodium carbonate. Johnson discloses that acidity of the hindgut was neutralised by administering sodium carbonate to the caecum not to the stomach. Accordingly, Pagan does not supplement the shortcomings of either Johnson or Winskill. It is respectfully submitted that none of the cited references, either alone or in combination, render obvious the presently-pending claims.

19. As discussed above, the Applicants believe the cited art contains no disclosure of a link between stomach condition and performance of stereotypies. Stomach and hind-gut acidity have a different chemical basis and are not dependent on each other. Knowledge of the link between hindgut acidity and abnormal behaviour in the cited art would not have led a

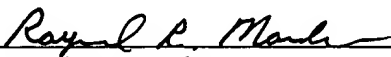
skilled artisan to prevent, reduce, or treat ulcers to prevent, treat, or ameliorate stereotypy by administering the compositions of the present invention to the stomach.

In relation to the administration of fat and fibre, please note the Applicants have shown in a study reported in the enclosed manuscript that a fat and fibre diet can be extremely effective in stopping stereotypic behavior. In the study, half of the crib-biting foals administered a fat and fibre diet stopped or reduced their crib-biting (see enclosed manuscript, page 7, last paragraph to page 8, first paragraph).

Wherefore, for all the reasons set forth above, it is respectfully submitted that the art of record does not disclose or suggest the presently claimed invention. Accordingly, it is respectfully requested that the claims be allowed and the case passed to issue.

Applicants' undersigned attorney may be reached in our New York office by telephone at (212) 218-2100. All correspondence should continue to be directed to our address given below.

Respectfully submitted,

  
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